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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,116	07/07/2003	Daniel A. Coleman	09367.00062-00000	9130
22852 7590 11/30/2007 FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP 901 NEW YORK AVENUE, NW WASHINGTON, DC 20001-4413			EXAMINER NEGIN, RUSSELL SCOTT	
			ART UNIT 1631	PAPER NUMBER
			MAIL DATE 11/30/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/615,116

Applicant(s)

COLEMAN ET AL.

Examiner

Russell S. Negin

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2007 and 07 September 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21,26,34,39-41,51-53 and 55-75 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21,26,34,39-41,51-53 and 55-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9/7/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Comments

Applicants' amendments and request for reconsideration in the communications filed on 1 June 2007 and 7 September 2007 are acknowledged and the amendments are entered.

Claims 21, 26, 34, 39-41, 51-53, and 55-75 are pending and examined in this Office action.

Information Disclosure Statement

The Information Disclosure Statement filed on 7 September 2007 has been considered.

Withdrawn Rejections

The rejection of claims 21, 42, 54, and 61-62 under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus [US Patent 4,741,043] is withdrawn in view of amendments filed on 7 September 2007.

Claim Objections

Claim 55 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. In this instance,

claim 55 is improperly dependent from a cancelled claim. Although claim 54 was originally dependent from claim 50, claim 50 is also a cancelled claim. For these reasons, it is not known from which claim instant claim 55 depends, and the examiner cannot make any interpretation for which of the various methods claimed is intended to be further limited by claim 55. For this reason, claim 55 will not be further treated on the merits.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26, 34, 39-41, 51-53, and 56-75 are rejected under 35 U.S.C. 101

because the claimed invention is directed to non-statutory subject matter.

The following analysis of facts of this particular patent application follows the analysis suggested in the "Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility". Note that the text of the Guidelines is italicized.

To satisfy section 101 requirements, the claim must be for a practical application of the § 101 judicial exception, which can be identified in various ways (Guidelines, p. 19):

- The claimed invention "transforms" an article or physical object to a different state or thing.
- The claimed invention otherwise produces a useful, concrete and tangible result.

In the instant case, the claimed invention does not “transform” an article or physical object to a different state or thing because the instantly rejected set of claims is drawn to methods for characterizing cells. This does not preclude the subject matter to be patentable as, for eligibility analysis, as

physical transformation “is not an invariable requirement, but merely one example of how a mathematical algorithm [or law of nature] may bring about a useful application.” AT&T, 172 F.3d at 1358-59, 50 USPQ2d at 1452. If the examiner determines that the claim does not entail the transformation of an article, then the examiner shall review the claim to determine if the claim provides a practical application that produces a useful, tangible and concrete result. In determining whether the claim is for a “practical application,” the focus is not on whether the steps taken to achieve a particular result are useful, tangible and concrete, but rather that the final result achieved by the claimed invention is “useful, tangible and concrete.” The claim must be examined to see if it includes anything more than a § 101 judicial exception. If the claim is directed to a practical application of the § 101 judicial exception producing a result tied to the physical world that does not preempt the judicial exception, then the claim meets the statutory requirement of 35 U.S.C. § 101. If the examiner does not find such a practical application, the examiner has determined that the claim is nonstatutory. (Guidelines, p. 20)

The question is thus whether the final result achieved by the claimed invention satisfies all three criteria of being useful, and concrete, and tangible.

Furthermore, the useful, tangible, and concrete result must be recited in the claim itself, rather than addressed in specification.

Instant claims 26, 34, 39-41, 51-53, and 55-58 and 60-75 are drawn to a method for assessing binuclear cells. However, as claimed, in an embodiment of the instant set of claims the method does not produce a tangible result. For example, the claimed method may be output to a computer memory device where events take place entirely within the confines of a computer or a human mind without any communication to the

outside world and without using or making available for use, the results of the computation. Thus, while the instant methods of the claims MAY produce a tangible result; i.e. output to a display, they also encompass nonstatutory embodiments wherein no tangible result is produced; i.e. output to a computer memory device. As the claims still encompass nonstatutory embodiments, the rejection is maintained.

Furthermore, instant claims 26, 34, 39, 51, and 59 do not produce a concrete result in that while the claims recite outputting of "at least one characteristic," it is not known which characteristic or characteristics listed in the set of claims are output to the display or memory device. If it is not known what the output result is, then the result cannot be reproduced. If the result is not reproducible, then it is not concrete.

Instant claims 59-60 are drawn to a computer program product and device for assessing binuclear cells. Applicant is reminded that a program and device, per se, are not automatically statutory subject matter. Rather, claims 59-60 are directed to nonstatutory subject matter for the same reasons as discussed above with respect to the method claims. See MPEP 2106. For example, the method on the computer program product as claimed may take place entirely within the confines of a computer without any communication to the outside world.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

35 U.S.C. 103 Rejection #1:

Claims 21 and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] in view of in view of Ravkin [WO 98/52018, issued 19 November 1998].

Claim 21 is drawn to a method for assessing the affect of a treatment on a population of cells comprising the following steps:

- exposing a population of cells to the treatment;
- capturing an image of a plurality of cells from the population;
- automatically obtaining a plurality of first cellular features from the image,

wherein the first cellular features are characteristic of a nuclear morphology property of the cells in the population;

--automatically analyzing the plurality of first cellular features and the plurality of second cellular features to automatically determine the abundance of bi-nuclear cells in the population; and

--automatically classifying the treatment based on the distribution of the nuclear morphology property, distribution of the inter-nuclear property, and abundance of bi-nuclear cells in the population;

--wherein the automatic classifying comprises comparing the distribution of the nuclear morphology property, distribution of the inter-nuclear property, and abundance of bi-nuclear cells in the population to a database of similar data derived from control untreated cells or cells subjected to a plurality of treatments; and

--wherein the treatment is classified in terms of its affect on cytokinesis.

The study of Gerlyng et al. investigates methods of study of liver cell proliferation.

Figure 1 on page 407 of Gerlyng et al. shows liver hepatocytes treated with dye and imaged (preamble and first two steps of the instant claim).

The morphology for the plurality of cells was analyzed and a "BrdUrd" index (column 1 of text of page 407 of Gerlyng et al.) was used to convert cells in the visual data comprising nuclear and cytoplasmic data to a statistic of percentage of cells that are bi-nuclear (Table 1 on page 207 of Gerlyng et al.) [third and fourth steps of instant claim 21]

In turn, these percentages of binuclear cells were classified into livers at different treatment stages (i.e. a regenerating liver and a normal liver; see Table 1 of page 407 of Gerlyng et al.; fifth step of instant claim 21).

As stated above, the results of Table 1 were obtained by classifying distribution of binuclear cells, which were based on nuclear morphological properties and internuclear properties in a control or regenerating liver. [sixth step of instant claim 21]

The binuclear data is based on cytokinesis in that the visual separation techniques rely not only on the presence of nuclei, but also on the presence of cytoplasm. [seventh step of instant claim 21]

Claim 61 is further limiting wherein the plurality of first cellular features includes nuclear features.

Claim 62 is further limiting wherein the plurality of second cellular features includes cytoplasmic features.

Figure 1 of Gerlyng et al. illustrates both nuclear and cytoplasmic features.

Gerlyng et al. does not show an automated means for obtaining the visual qualitative data.

The patent of Ravkin identifies fetal red blood cells using the automated device shown on the cover figure of the patent.

It would have been obvious to someone of ordinary skill in the art at the time of invention to obtain the cell images in the assays of Gerlyng et al. via automation using the computer apparatus of Ravkin where the motivation would have been that automating a known manual technique results in a more expeditious and accurate procedure (see, for example, cover figure of Ravkin).

35 U.S.C. 103 Rejection #2:

Claims 26, 59-60, and 63-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cambier et al. [Acta Cytologica, 1978, volume 22, pages 523-529] in view of Ravkin [WO 98/52018, issued 19 November 1998].

Claim 26 is drawn to a method for characterizing cells, comprising; automatically determining from a captured image of a nuclear component of a plurality of cells, the number of concave portions in the outline of the image of the nuclear component, wherein a concave portion in the outline of the image of the nuclear component is identified by automatically determining the angle subtended by adjacent portions of the outline, wherein identifying a concave portion further includes determining whether the angle is less than a threshold angle; and automatically characterizing the cell based on the number of concave portions; wherein at least one determined characteristic of the cells is outputted to at least one display or memory device.

Claims 59-60 are drawn to a computer program product and device comprising a machine readable medium on which there is code for;

- identifying from the captured image at least one pair of nuclear components;
- identifying from the captured image a nearest neighbor nuclear component to the pair of nuclear components;
- characterizing the cell associated with the pair of nuclear components based on separation of the pair of nuclear components and the separation of the nearest next neighbor nuclear component from the pair of nuclear components.

Cambier et al. studies binuclear cell recognition of binuclear cells from the uterine cervix.

Figure 1 of Cambier et al. illustrates an image of a binuclear cell with concave and convex portions on the outlines of the image. The last full paragraph of page 524 and the paragraph bridging pages 524-525 of Cambier et al. describes the parameters (i.e. TCD, MCD, P2A, and RPS) with threshold values used to quantify the concave properties of the cell image based on angles, areas, and perimeter of and within the image with threshold values indicating the boundary between a normal cell and a binuclear cell.

Figure 2 of Cambier et al. illustrates the threshold in a histogram of overall intensities comparing bi-nuclear to mono nuclear cells with the help of a first threshold value within the histogram.

Figure 2 of Cambier et al. also illustrates a scheme of two nearest neighbors which constitute a binuclear and mononuclear cell, respectively.

Claim 63 is further limiting wherein the image of the cell is smoothed. Claim 64 is further limiting wherein the outline of the image involves converting the image to a polygon. Figure 8 on page 528 of Cambier et al. illustrates the smoothing of an image using a polygon outline.

Claim 65 is further limiting wherein the cell is automatically characterized based on the number of concave portions identified and a second criterion. Claim 66 limits this second criterion to be indicative of the amount of nuclear material.

The last full paragraph of page 524 and the paragraph bridging pages 524-525 of Cambier et al. describes the parameters (i.e. TCD, MCD, P2A, and RPS) with threshold values used to quantify the concave properties of the cell image based on angles, areas, and perimeter of and within the image with threshold values indicating the boundary between a normal cell and a binuclear cell. In addition to perimeters, and concavities, other parameters such as area are evaluated to characterize the specific cells.

The study of Cambier et al. does not teach automated analysis of the binuclear assessments performed.

The patent of Ravkin identifies fetal red blood cells using the automated device shown on the cover figure of the patent.

It would have been obvious to someone of ordinary skill in the art at the time of invention to obtain the cell images in the analysis of Cambier et al. via automation using the computer apparatus of Ravkin where the motivation would have been that automating a known manual technique results in a more expeditious and accurate procedure (see, for example, cover figure of Ravkin).

Claims 34, 41, 51-53, 56-58, and 67-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cambier et al. in view of Ravkin as applied to claims 26, 59-60, and 63-66 above, and further in view of Gerlyng et al..

Claim 34 is drawn to the same subject matter as claim 26 with the further limitations of not only a first threshold to compare normal cells to binuclear cells, but also a second threshold with which to compare binuclear cells to multinucleate cells.

Claim 41 is further limiting wherein the amount of cytoplasmic component is automatically determined by summing over the peripheries of the nuclear components.

Claim 51 is drawn to the same subject matter as claim 26 with the additional limitation of using nearest neighbors, instead of concavity to determine the thresholds between mononuclear, binuclear, and multinuclear cells.

Claim 52 is further limiting where the second threshold is at least twice the first threshold.

Claim 56 is further limiting wherein the first and second thresholds are computed based on densities of nuclear components in the captured images.

Claim 57 is further emphasizes the relation between the first and second thresholds and the nearest neighbor nuclear components.

Claim 58 is further limiting where in the proportion of binuclear cells are determined.

Claims 67 and 70 are further limiting wherein the cell is characterized as multinuclear if more than two concave portions are identified.

Claim 68 is further limiting wherein characterizing the cell further includes assessing a further feature of a nuclear image of the nuclear component.

Claim 69 is further limiting wherein the further feature of the image is the total intensity of the image of the nuclear component.

Cambier et al. in view of Ravkin make obvious an automated method for determining mononuclear cells in a population of cells. Cambier et al. calculates the peripheries around the nuclei which are interpreted to be used to teach the degree of binucleation in the sample (i.e. claim 41). Furthermore Figure 2 of Cambier et al. plots out nearest neighbor pairs of nuclei (i.e. claim 57).

Cambier et al and Ravkin do not teach a second threshold for multinuclear cells.

The study of Gerlyng et al. investigates methods of study of liver cell proliferation.

Gerlyng et al. teaches additional thresholds with additional types of multinuclear cells in Figure 3 on page 409 (i.e. claims 34 and 51). The second threshold is interpreted to be twice as large as the first threshold. (i.e. claim 52) The cells that have more the two nuclei have more than two concave sections (i.e. claims 67, 68 and 70). Gerlyng et al. also teaches the proportion of normal to binuclear cells in liver in Table 1 (i.e. claim 58) based on nuclear images, densities and intensities of the hepatocytes (i.e. claims 56 and 69).

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the graphical cellular imaging algorithms made obvious by Cambier et al. and Ravkin with the threshold model of Gerlyng et al. where the

motivation would have been to add additional detail to additionally detect higher numbers nuclei within a single cell (see for example, Figure 3 of Gerlyng et al.).

Response to Arguments

Applicant's arguments with respect to claims 21, 42, 54, 61, and 62 have been considered but are moot in view of the new ground(s) of rejection.

It is noted the study of Gerlyng et al. is sustained from the previous Office action. Since it is agreed that Gerlyng et al. does not teach the automated method, but instead teaches a manual technique, the patent of Ravkin is relied upon for a teaching of automation.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RSN
26 November 2007

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/Marjorie A. Moran/
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11/26/2007